Sinonasal Mucosal Malignant Melanoma: Report of an Unusual Case Mimicking Schwannoma

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Primary mucosal melanoma of the sinonasal tract is a rare malignancy that has a more aggressive clinical course than its cutaneous counterpart. The histology of these lesions varies, with differing degrees of melanin production and an epithelioid or spindle-cell growth pattern. Cutaneous melanocytic lesions may differentiate in accordance with their neural crest derivation and express morphology similar to nerve sheath tumors. We believe the following case study reports the first instance of a mucosal melanoma with a Schwannian pattern of growth, arising from the nasal cavity of a 26-year-old man.
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PRIMARY mucosal melanoma of the head and neck is an uncommon neoplasm that represents 0.5 to 2% of all malignant melanomas, and is clinically more aggressive than its cutaneous counterpart with a 5-year survival rate of 10% to 38%.[1] Specifically, sinonasal tumors account for <1% of all malignant melanomas and have a 5-year survival rate of 0% to 30%.[2] Melanoma is characterized by a protean histologic growth pattern, although most commonly epithelioid or spindled. Rare cases of neurotropic melanoma are described,[3-9] with the skin of the head and neck the most commonly reported site of occurrence. Bearing the rarity of this tumor in mind, we report a unique case of a primary mucosal melanoma of the nasal cavity with a growth pattern that mimics schwannoma.

Case Report

A 26-year-old white man with a long history of allergies and sinus problems presented with nasal obstruction. He reported an intermittent history of severe epistaxis since childhood, which had decreased in severity and frequency as he had grown older. He had been a ''mouth breather'' all of his life. He had no symptoms of facial pain or pressure, sneezing, rhinorrhea, watery or itchy eyes, hoarseness, or dysphagia, but did report mild anosmia. He was being treated with loratadine and triamcinalone acetamide nasal spray without any symptomatic relief.

Physical examination revealed a large polypoid mass with prominent vasculature that completely filled the left nasal cavity and descended around the choanae, partially filling the posterior aspect of the right nasal cavity. Computed tomography revealed a 4-cm ovoid soft tissue mass within the left nasal cavity. The mass, enhanced with contrast, partially eroded the inferior turbinate and obliterated the middle turbinate. The bony nasal septum was slightly bowed to the right. The left maxillary antrum showed prominent mucosal thickening and fenestration of the medial wall. The left frontal sinus was partially opacified with mucosal thickening and air-fluid levels. The mass was subsequently excised with the clinical impression of an antrochoanal polyp.

The specimen was composed of multiple fragments of fleshy, tan-yellow to reddish-gray soft tissue, the largest of which measured 3 cm in greatest dimension. The cut surfaces of the fragments were focally hemorrhagic, smooth, nodular, gray-tan to pale yellow.

Low-power microscopic examination revealed multiple fragments of a submucosal, unencapsulated but somewhat circumscribed spindle cell neoplasm (Fig 1). The spindled cells were arranged in short intersecting fascicles with areas of nuclear palisading and associated eosinophilic stromal matrix, reminiscent of the cellular Antoni A areas of a schwannoma. On higher power microscopic examination the tumor was composed of cells with enlarged and plump ovoid to spindled nuclei

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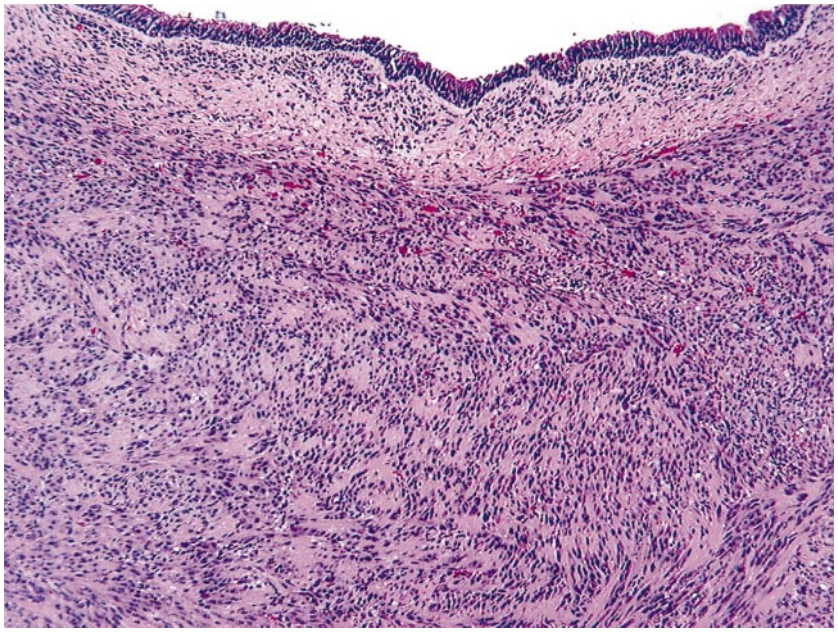

Figure 1. Submucosal spindle cell tumor exhibiting a schwannoma-like pattern of growth.

with blunted ends, accentuated and irregular nuclear membranes, and vesicular nuclear chromatin. The majority of the cells contained prominent and irregular eosinophilic nucleoli (Fig 2). Mitotic figures were present, but rare.

The tumor cells reacted strongly with immunohistochemical antibodies for S-100 protein and HMB-45 and were negative with keratin, smooth muscle actin, and glial fibrillary acidic protein (Fig 3). Collagen type IV was deposited around the tumor cells. Electron microscopic examination of the tumor revealed abundant intercellular collagen with absent basement membrane reduplication. Helical premelanosomes were identified (Fig 4).

The patient subsequently underwent a subtotal maxillectomy, followed by a course of radiation therapy. He is presently free of disease 6 months after the initial biopsy.

Discussion

Malignant melanoma of the sinonasal tract is a rare and aggressive disease which, in the majority of cases, is

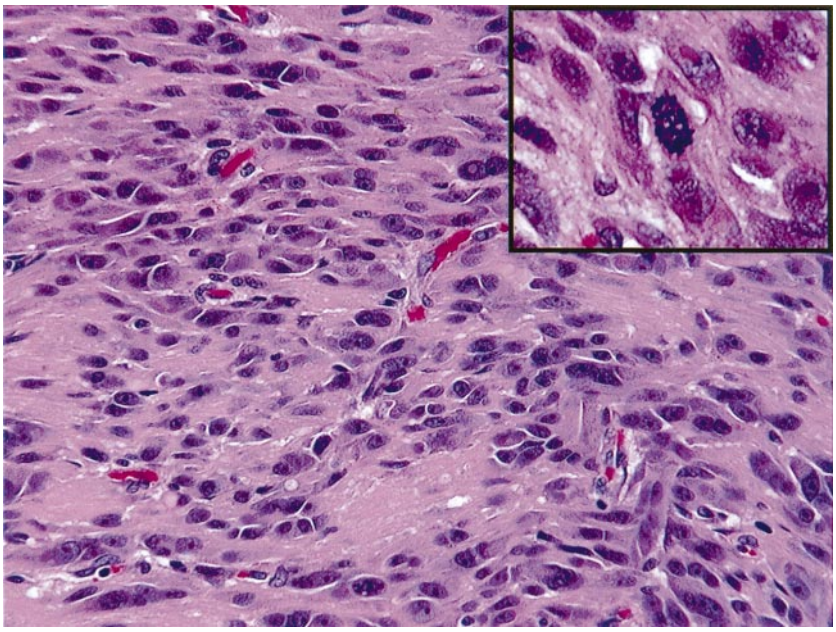

Figure 2. High power microscopic examination showing nuclear pleomorphism, prominent nucleoli, intranuclear cytoplasmic inclusions, and rare mitotic figures (inset).

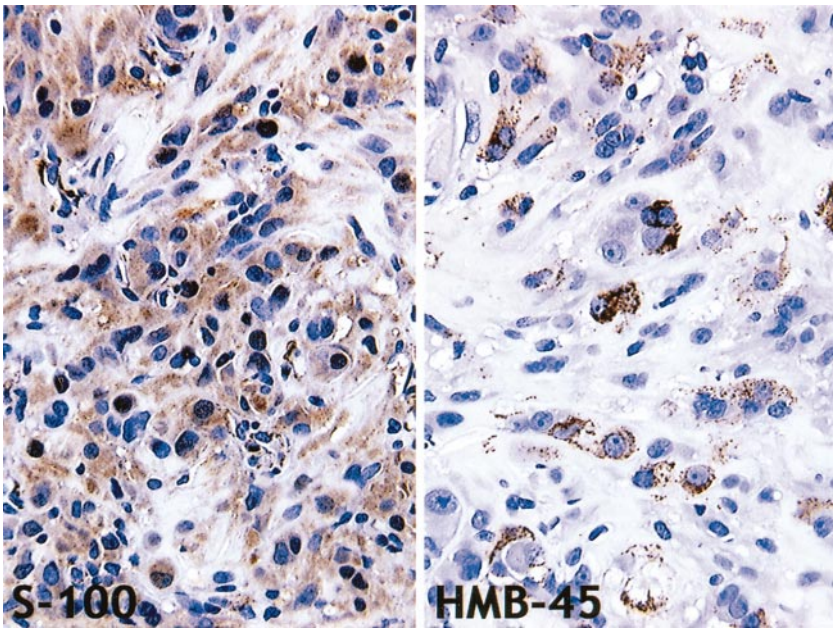

Figure 3. Immunohistochemical nuclear reactivity for S-100 protein (left) and cytoplasmic granular reactivity for HMB-45 (right).

lethal within five years. The nasal cavity is more commonly the site of origin than are the paranasal sinuses, but tumors frequently involve both locations by the time they are discovered.[10] When the sinuses are the primary site, the maxillary sinus is more commonly involved than the ethmoid sinus. Origin from the frontal or sphenoid sinuses is rare.[11] Patients typically present in the sixth to eighth decades of life, but these lesions occur over a wide age range.[10] Mucosal melanomas behave unpredictably; some tumors have a rapid clinical course, while others lie dormant for over 10 years after resection before recurring or metastasizing. One relatively consis-

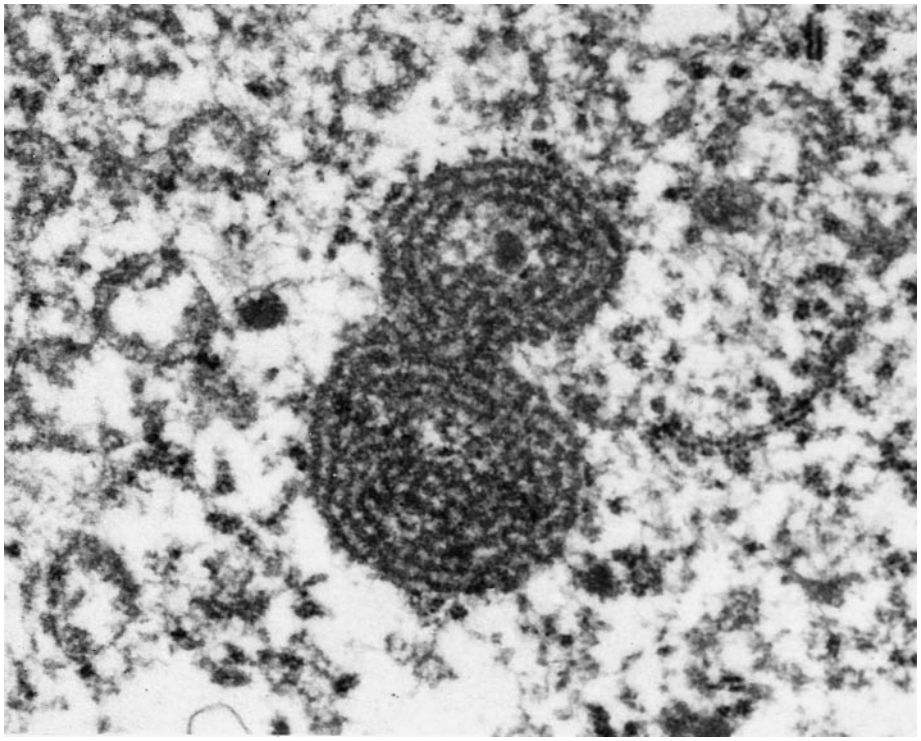

Figure 4. Rare helical premelanosome. (Original magnification ×48,000).

tent feature is that the disease tends to recur locally before metastasizing to distant sites.[2] Many investigators believe that all mucosal melanomas are eventually lethal, and have stated that treatment is merely palliative.[12,13] However, some patients do survive for a long period of time following surgery, and a few studies suggest that even though melanoma is usually considered radioresistant, the addition of radiation therapy following surgery may prolong survival.[2]

Mucosal malignant melanomas originate from melanocytes, which are present in mucosal linings throughout the body. Clearly sunlight exposure is not a major risk factor for melanomas originating in these locations as it is in the skin. However, there are significant racial differences in the incidence of mucosal melanomas: whites in the United States have a three-fold higher risk for developing melanoma in sites other than the skin or eye. In Japan oral melanoma is relatively common, accounting for up to 7.5% of all melanomas.[1,14] While most of the Japanese patients have associated melanosis of the oral cavity, a similar incidence is not seen in blacks, among whom pigmentation of the oral cavity is a common phenomenon. Since the clinical setting and epidemiology is so divergent from that seen in cutaneous melanomas, the pathogenesis and etiology of mucosal melanoma remains poorly understood.

Sinonasal malignant melanoma may be sessile or polypoid and is frequently ulcerated. Like its cutaneous counterpart it may be a variety of different colors, including white, pink, brown, or black. Histologic diagnosis is generally not problematic, since the majority of these tumors produce melanin pigment in varying amounts. The malignant cells are either epithelioid or spindled and characteristically have enlarged and pleomorphic vesicular nuclei with prominent nucleoli. Necrosis and increased mitotic activity with atypical mitotic figures are commonly present. Diagnostic difficulty occurs in 10% to 30% of melanomas that are amelanotic. Diagnosis in these cases requires a high index of suspicion, as both the epithelioid and spindle cell melanomas may mimic other malignancies that occur in this location. Ancillary studies are of great utility in these circumstances. Immunohistochemical stains for S-100 protein, HMB-45, melan-A, and tyrosinase are characteristically positive and electron microscopy typically reveals cytoplasmic melanosomes or pre-melanosomes.

This case demonstrates an unusual histologic morphology mimicking that of a schwannoma. This phenomenon has been described in melanomas of the skin,[3,4,6] particularly with desmoplastic melanoma. The expression of a neurogenic morphology within melanocytic lesions is due to the common embryologic origin from the neural crest of both melanocytes and Schwann cells. This phenotypic overlap is seen within melanocytic nevi, which frequently mature or neuritize toward the base of the lesion within the dermis.

Neurotropic malignant melanoma is the term used for a subset of desmoplastic melanomas that invade and extend along peripheral nerves. They typically arise on the skin of the head and neck, often lack an intraepidermal component, and occasionally extend along peripheral nerves for significant distances. Both desmoplastic and neurotropic melanomas frequently resemble neural tumors histologically, tending to form nerve-like cell bundles accompanied by a pericellular basement membrane.[15] Whereas there has been a single case[16] described in the literature originating on the buccal mucosa, to the best of our knowledge, based on a review of the English literature (MEDLINE 1960-2000[17]), we are reporting the first instance of a sinonasal melanoma with a neuroid growth pattern.

The foremost entity in the differential diagnosis for this case is malignant peripheral nerve sheath tumor (MPNST). The distinction between MPNST and melanoma may be difficult. This confusion may have led to the erroneous diagnosis of cutaneous desmoplastic melanoma as MPNST in earlier case reports.[16] Features in favor of malignant melanoma are larger nuclei, prominent eosinophilic nucleoli, amphophilic cytoplasm, diffuse immunoreactivity for S-100 protein and HMB-45, and the ultrastructural presence of melanosomes or pre-melanosomes. Clinically, the distinction between MPNST and melanoma is important. While both tumors have a poor prognosis, the prognosis for mucosal melanoma is worse, necessitating differences in the treatment regimens used during the often aggressive and tenacious clinical course. Treatment, among those who advocate attempts at therapy beyond palliation, involves radical extirpation with or without postoperative radiation therapy. A few studies suggest that margins of resection may not play a large role in predicting recurrence or metastasis, as the incidence of recurrence is high even with negative surgical margins.[2] Therefore, excision of apparently uninvolved anatomic structures in an attempt to assure wide surgical margins must be carefully balanced with preservation of function.

We describe an unusual morphology of a primary mucosal melanoma of the nasal cavity, which emphasizes the importance of suspecting malignant melanoma when confronted with a spindle cell or poorly differentiated sinonasal tumor. Nearly one-third of mucosal

melanomas produce no appreciable pigment and ancillary studies are requisite for diagnosis. Differentiation from other neural tumors is important for appropriate clinical management.

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